

### REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

#### Interview Summary

Applicants wish to thank Examiners Nguyen and Angell for extending the courtesy of discussing this application with inventor Matt Coffey as well as Applicants' representatives Mary Ann Dillahunt and Ping Hwung in a personal interview on February 18, 2005. No exhibit was presented. Applicants proposed to incorporate the claim elements of claim 14 into claim 1 and discussed the reasons why it would not have been obvious to combine the base administration of claim 1 and the additional administrations of claim 14. The Examiners recommended that claim 1 be amended to recite "oncolytic virus" and "multiple intratumor injections on the same day". The amendments and arguments presented herein are made in accordance with these discussions.

#### Claim Amendments

Claims 14 and 17-21 have been canceled without prejudice or disclaimer.

Claim 1 has been amended to incorporate the claim elements of claim 14. Accordingly, claim 14 has been canceled, and claims 15 and 16 have been amended to depend from claim 1 instead of claim 14.

Claim 1 has also been amended to recite "an oncolytic virus" and "multiple intratumor injections", for which support can be found, for example, at page 13, lines 14-19 and in Example 2 (page 21), respectively.

Claims 8-13 have been amended to recite "in the base administration" for clarity in view of the amendments in claim 1.

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Applicants submit that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence to any rejections or ground of unpatentability. Applicants reserve the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

Rejection Under 35 U.S.C. §103

The rejection of claims 1-21 under 35 U.S.C. §103(a) as allegedly unpatentable over Lee et al. (WO 99/08692) in view of Heise et al. (Cancer Gene Therapy 6(6):499-504, 1999) is respectfully traversed for the reasons set forth below.

To properly issue a rejection under 35 U.S.C. §103, the USPTO bears the initial burden to establish a prima facie case of obviousness by meeting three criteria. One of the criteria is that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at the claimed invention. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991).

As amended, claim 1 is directed to a method for delivering an oncolytic virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of the virus to a subject bearing the tumor, wherein the virus is capable of selectively killing cells of the tumor, by

(1) a base administration of multiple intratumor injections on the same day of a composition comprising the virus, wherein the volume of the composition injected per site is between about 10% to about 100% of the volume of the tumor; and

- (2) at least one additional administration selected from the group consisting of:
- (a) delivering the virus by using a transdermal patch, a spray on the skin, or topical administration, wherein the tumor is a superficial tumor; and
  - (b) delivering the virus systemically.

A skilled artisan would not have been motivated by the cited references to combine the base administration with the additional administration of the claimed invention. Lee et al. teach the use of reovirus in reducing tumor growth. With respect to the mode of delivery, Lee et al. teach that for a solid neoplasm that is accessible, the reovirus can be injected directly into the neoplasm (page 8). For neoplasms that are not easily accessible within the body, such as metastases or brain tumors, the reovirus can be administered systemically (pages 8-9). Lee et al. further teach that "[A]lternatively, the reovirus can be administered directly to a single solid neoplasm, where it then is carried systemically through the body to metastases" (page 9). Therefore, Lee et al. do not specifically teach or suggest the desirability of combining intratumor injections and systemic delivery. Heise et al. teach the impact of intratumoral spread and distribution on the efficacy of ONYX-015 therapy. However, Heise et al. also do not teach or suggest combining intratumor injections and systemic delivery. Similarly, neither reference teaches or suggests the combination of intratumor injections and a transdermal patch/ spray on the skin/topical administration as recited in claim 1. Therefore, there is no suggestion or motivation to modify the teachings of the cited references, either alone or in combination, to arrive at the claimed invention. Accordingly, the claimed invention is not obvious.

If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); MPEP 2143.03. Since all the other currently pending claims ultimately depend from claim 1, all of these claims are nonobvious.

Accordingly, withdrawal of this rejection is respectfully requested.

Applicant : Coffey et al.  
Serial No. : 09/987,687  
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Attorney's Docket No.: 16596-015001

Conclusions

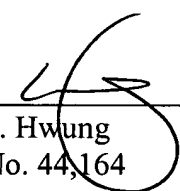
For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Enclosed is a \$225.00 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: May 9, 2005

  
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